Exhibit A

Invalidity Chart for the ’726 Patent
(’538 Patent in view of Wong and/or the ’056 Patent)

INVALIDITY CLAIM CHART A
U.S. PATENT NO. 5,686,726 ('538 Patent in view of Wong and/or '056 Patent)

The '726 patent is invalid for obviousness-type double patenting over U.S. Patent No. 5,130,538 to Fenn et al. ("the '538 patent"), either alone or in view of U.S. Patent No. 4,531,056 to Labowsky et al. ("the '056 patent") and/or in view of Wong, *Multiple Charging in Electrospray Ionization of Poly(ethylene glycols)*, 92 J. Phys. Chem. 546-50 (1988) ("Wong article").

5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
Claim 1	Claim 1 in view of claims 20 and 38 of the '538 patent or Claim 1 in view of Wong	
A composition of matter comprising a population of multiply charged polyatomic ions derived from a distinct polyatomic parent molecular species, all molecules of said distinct polyatomic parent molecular species having substantially the same molecular weight and chemical identity, the number of charges on each ion in said population of multiply charged polyatomic ions defining that ion's charge state number, said population of multiply charged polyatomic ions comprising a plurality of sub-populations of ions, all the ions of each of said sub-populations having the same charge state number,	(claim 1) A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, (claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species; . . . (claim 1 cont'd) the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number,	Claim 1 of the '726 patent differs from claim 1 of the '538 patent in that claim 1 of the '726 patent recites that all the molecules of the polyatomic parent molecular species have substantially the same chemical identity. Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same chemical identity. *See* Wong at 550. In fact, Wong, which is a prior art publication describing the application of electrospray ionization techniques to solutions of polyethylene glycols, states that, "[i]n future experiments, we plan to use relatively pure samples of known molecular weight." *Id.* Claim 1 of the '726 patent also differs from claim 1 of the '538 patent in that claim 1 of the '726 patent recites that the molecules of the species of each subpopulation of ions have the "same charge state number differing from the charge state numbers of the ions in the other sub-populations of said plurality of subpopulations." Not only is this disclosed by claim 38 of the '538 patent where it describes the ions in neighboring peaks (i.e. different sub-populations) as differing by one charge, but Wong also shows at Fig. 7 mass spectra for oligomers

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said same charge state number differing from the charge state numbers of the ions in the other sub-populations of said plurality of subpopulations, said plurality of sub-populations comprising one sub-population for each value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five.	(claim 38, depends from claim 34) . . . wherein said step of analyzing said sequence of discrete peaks of said spectrum includes uses the mass/charge (m/z) values of at least two of said peaks in said sequence of discrete peaks, said sequence of discrete peaks having a coherence whereby the ions of any arbitarily [sic] chosen one of said peaks in said sequence differ by one charge from the ions of the nearest peak whose ions are derived from identical molecules of the same said distinct polyatomic parent molecular species. (claim 1 cont'd) said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	with different charges for different peaks.
Claim 3, depends from claim 1	Claim 1 of the '538 patent	
The composition of matter of claim 1 in which said smallest value of charge state number is not less than seven and said largest value is not less than ten.	(claim 1) . . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five	Claim 3 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 3 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
Claim 5, depends from claim 1	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 1 in which said polyatomic parent molecular species is selected from a class of compounds known as biopolymers.	(claim 21, depends from claim 20) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 5 of the '726 patent specifies that the "polyatomic parent molecular species" is a biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents indicates that the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 6, depends from claim 1	Claim 1 in view of claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 1 in which said distinct polyatomic parent molecular species is not a synthetic polymers [sic] such as a poly (ethylene glycol), having less than four different constituent elemental species.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species	Claim 6 of the '726 patent excludes compounds such as PEG from claim 1. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 8, depends from claim 1	Claim 1 in view of claim 20 of the '538 patent or Claim 1 in view of the '056 patent	
The composition of matter as claimed in claim 1 in which said distinct polyatomic	(claim 20) A method for producing a population of multiply charged	Claim 8 of the '726 patent adds that distinct polyatomic parent molecular species has "molecular weight not less than 5000." Based on the specifications of both patents,

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parent molecular species has a molecular weight not less than 5000.	ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000	the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* '538 Patent at 4:42-58. Moreover, claim 20 of the '538 patent specifically recites the same limitation of "at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000." Furthermore, the '056 patent teaches "the electrospray technique produces ions from solutes of very high molecular weights (e.g. 500,000)." *See* '056 Patent at 3:7-14.
Claim 9	Claim 1 in view of claim 20 of the '538 patent or Claim 1 in view of the '056 patent	
A composition of matter comprising one or more populations of multiply charged polyatomic ions derived from a sample comprising at least one polyatomic parent molecular species, the number of charges on each ion defining said ion's charge state number, said population of multiply charged polyatomic ions formed from said at least one polyatomic parent molecular species comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number,	A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number,	Claim 9 of the '726 patent differs from claim 1 of the '538 in that claim 9 of the '726 patent recites steps related to the process by which the claimed compositions are generated. But the addition of a process or source limitation does not make a composition claim patentable if the composition itself is, as here, already in the prior art. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985); *see also* M.P.E.P. § 2113. Moreover, the electrospray ionization steps are recited by claim 20 of the '538 patent. And the added process steps were known in the electrospray mass spectrometry art. *See, e.g.,* '056 Patent at 2:53-60.

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said charge state number differing by one from the next largest and the next smallest values of charge state number found in the other sub-populations of said plurality,	said population including one sub-population for each possible integral value of charge state number	
the ions of each of said sub-populations having a value of said charge state number that is not less than five, said composition of matter being formed by:	extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations. ---------- (claim 20) A method for producing a population of multiply charged ions . . . comprising the steps of: . . .	
dispersing a solution of said sample containing said at least one polyatomic parent molecular species into a bath gas as charged droplets, said dispersing taking place in the presence of an electric field; and	dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and	
allowing the solvent of said solution to evaporate from said charged droplets until at least some molecules of said polyatomic parent molecular species become dispersed in said bath gas as said multiply charged polyatomic ions.	allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions.	

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5,686,726	**'538 Patent**	**Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)**
Claim 10, depends from claim 9	Claim 1 of the '538 patent	
The composition of matter of claim 9 in which the charge state number of the ions in each of said sub-populations of said plurality of sub-populations is at least seven.	(claim 1) . . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five	Claim 10 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 10 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 11, depends from claim 9	Claim 1 in view of Claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 9 in which all molecules of said at least one of said polyatomic parent molecular species have substantially the same molecular weight.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species	Claim 11 of the '726 patent recites that all the molecules of the species have "substantially the same molecular weight." Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same molecular weight. *See* Wong at 550.
Claim 16	Claim 1 of the '538 patent	
A composition of matter comprising one or more distinct populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species, the number of charges on each ion defining the ion's charge state	A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number,	Each element of claim 16 of the '726 patent is found in claim 1 of the '538 patent.

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number, each of said populations of polyatomic ions comprising a plurality of sub-populations, each of said plurality of sub-populations being comprised of ions formed from one of said distinct polyatomic parent molecular species and having the same charge state number, there being at least one of said populations of multiply charged polyatomic ions that comprises one of said sub-populations for each value of charge state number beginning with a smallest value of three and extending to a largest value not less than five.	said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	
Claim 18, depends from claim 16	Claim 1 of the '538 patent	
The composition of matter of claim 16 in which said smallest value of charge state number is not less than seven and said largest value of charge state number is not less than ten.	(claim 1) . . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five;	Claim 18 of the '726 patent differs only from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 18 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 19, depends from claim 16	Claim 1 in view of Claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim	(claim 20)	Claim 19 of the '726 patent adds that all the

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16 in which all molecules of each of said distinct polyatomic parent molecular species have substantially the same molecular weight.	A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species	molecules of the species have "substantially the same molecular weight" to claim 16. Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same molecular weight. *See* Wong at 550.
Claim 20, depends from claim 16	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter in claim 16 in which at least one of said distinct polyatomic parent molecular species is selected from a class of compounds known as biopolymers.	(claim 21, depends from claim 20) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 20 of the '726 patent specifies that the "polyatomic parent molecular species" is a biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents suggests the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 21, depends from claim 16	Claim 1 in view of Claim 27 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter in claim 16 in which at least one of said distinct polyatomic parent molecular species is selected from the group comprising proteins, peptides, polypeptides, carbohydrates,	(claim 27, depends from claim 26, which depends from claim 20) . . . wherein at least one of said distinct polyatomic parent molecular species is chosen from the class known as biopolymers and comprising peptides, proteins, glycoproteins, carbohydrates and polynucleotides.	Claim 21 of the '726 patent adds to claim 16 that parent molecular species are "proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins." Not only does claim 27 of the '538 patent recite precisely this limitation, but such compounds are simply examples of the biopolymers disclosed by the '056 patent. *See* '056

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oligonucleotides and glycoproteins.		Patent at 3:7-14.
Claim 22, depends from claim 16	Claim 1 in view of claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 16 in which at least one of said distinct polyatomic parent molecular species is not a synthetic polymer, such as a poly (ethylene glycol), having less than four different constituent elemental species.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species;	Claim 22 of the '726 patent excludes compounds such as PEG from claim 16. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 23, depends from claim 16	Claim 1 in view of claim 20 of the '538 patent or Claim 1 in view of the '056 patent	
The composition of matter of claim 16 in which at least one of said distinct polyatomic parent molecular species has a molecular weight not less than about 5000.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species. . . .	Claim 23 of the '726 patent adds that the polyatomic parent molecular species has a "molecular weight not less than about 5000." Based on the specification of both patents, the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* '538 Patent at 4:42-58. Moreover, claim 20 of the '538 patent specifically recites the similar limitation of "at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000." Furthermore, the '056 patent teaches "the electrospray technique produces ions from solutes of very high molecular weights (e.g. 500,000)." *See* '056 Patent at 3:7-14.

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5,686,726	’538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the ’056 patent)
Claim 24	Claim 1 of the ’538 patent	
A composition of matter comprising one or more distinct populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species, the number of charges on each ion defining its charge state number, each of said populations of multiply charged polyatomic ions comprising ions formed from one of said distinct polyatomic molecular species and being comprised of a plurality of sub-populations, the ions of each of said sub-populations having the same charge state number, there being one of said sub-populations for each value of said charge state number beginning with a smallest value not less than three and extending to a largest value not less than five.	(claim 1) A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	Each element of claim 24 of the ’726 patent is found in claim 1 of the ’538 patent.
Claim 26, depends from claim 24	Claim 1 in view of claim 21 of the ’538 patent or Claim 1 of the ’538 patent in view of the ’056 patent	
The composition of matter of claim 24	(claim 21, depends from 20)	Claim 26 of the ’726 patent specifies that the “polyatomic parent molecular species” is a

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in which at least one of said distinct polyatomic parent molecular species is selected from a class of compounds known as biopolymers.	. . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents indicates that the term "polyatomic parent molecular species" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 27, depends from claim 24	Claim 1 in view of Claim 27 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 24 in which at least one of said distinct polyatomic parent molecular species is selected from the group comprising proteins, peptides polypeptides, carbohydrates, oligonucleotides and glycoproteins.	(claim 27, depends from 26, which depends from 20) . . . wherein at least one of said distinct polyatomic parent molecular species is chosen from the class known as biopolymers and comprising peptides, proteins, glycoproteins, carbohydrates and polynucleotides.	Claim 27 of the '726 patent adds to claim 24 that parent molecular species are "proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins." Not only does claim 27 of the '538 patent recite precisely this limitation, but such compounds are simply examples of the biopolymers disclosed by the '056 patent. *See* '056 Patent at 3:7-14.
Claim 28, depends from claim 24	Claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 24 in which at least one of said distinct polyatomic parent molecular species is not selected from the group comprising synthetic polymers having less than four different constituent elemental species, said group comprising poly (ethylene glycol)s.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species . . .	Claim 28 of the '726 patent excludes synthetic polymers such as PEG from claim 24. Claim 20 of the '538 patent also excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.

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Claim 29, depends from claim 24	Claim 20 of the '538 patent Claim 1 in view of the '056 patent	
The composition of matter of claim 24 in which at least one of said distinct polyatomic parent molecular species has a molecular weight not less than 5000.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species. . . .	Claim 29 of the '726 patent adds that the polyatomic parent molecular species has a "molecular weight not less than 5000." Based on the specification of both patents, the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* '538 Patent at 4:42-58. Moreover, claim 20 of the '538 patent specifically recites the same limitation— "at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000." Furthermore, the '056 patent teaches "the electrospray technique produces ions from solutes of very high molecular weights (e.g. 500,000)." *See* '056 Patent at 3:7-14.
Claim 31	Claim 1 in view of Claim 20 of the '538 patent or Claim 1 in view of the '056 patent	
A composition of matter comprising one or more distinct populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species, the number of charges on each ion defining the ion's charge state number, each of said populations of multiply	A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-	Claim 31 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Claim 1 of the '538 patent recites a charge state number "from a minimum of three to a maximum not less than five" and, as a species, anticipates claim 31, which recites "not less than three." *See In re Goodman*, 11 F.3d 1046, 1053 (Fed. Cir. 1993) (an earlier species claim anticipates and is therefore not patentably distinct from a later genus claim). Additionally, where the range recited in a claim overlaps or lies within the prior art, a

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charged polyatomic ions comprising ions formed from one of said distinct polyatomic parent molecular species in said sampler [sic] at least one of said populations of multiply charged polyatomic ions being comprised of a plurality of sub-populations, the ions of each of said sub-populations having the same value of charge state number, that value being different from the values of charge state number in all the other sub-populations of ions in said plurality of sub-populations, the smallest value of charge state number of the ions in said plurality of sub-populations being not less than three, said composition of matter being formed by: dispersing a solution containing said one or more distinct polyatomic parent molecular species into a bath gas as charged droplets, said dispersing taking place in the presence of an electric field. allowing the solvent of said solution to evaporate from said charged droplets until at least some molecules of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions.	populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations. ---------- (claim 20) A method for producing a population of multiply charged ions . . . comprising the steps of: . . . dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions.	prima facie case of obviousness exists and claim 31 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382. Claim 31 of the '726 patent also differs from claim 1 of the '538 in that claim 31 of the '726 patent includes steps related to the process by which the claimed compositions are generated. But the addition of a process or source limitation does not make a composition claim patentable if the composition itself is, as here, already in the prior art. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985); *see also* M.P.E.P. § 2113. Moreover, the Electrospray Ionization steps are recited by claim 20 of the '538 patent. The added process steps were also known in the electrospray mass spectrometry art. *See, e.g.,* '056 Patent at 2:53-60.

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Claim 33, depends from claim 31	Claim 1 of the '538 patent	
The composition of matter of claim 31 in which said smallest value of charge state number is not less than seven.	(claim 1) . . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five	Claim 33 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 33 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 35, depends from claim 31	Claim 1 of the '538 patent alone or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 31 in which all molecules of at least one of said distinct polyatomic parent molecular species have the same chemical formula.	(claim 1) . . . generating a population of multiply charged ions from a distinct polyatomic parent molecular species,	Claim 35 of the '726 patent recites that "distinct polyatomic parent molecular species have the same chemical formula," another way of stating that the molecules of the distinct parent molecular species have substantially the same molecular weight or formula or be otherwise indistinguishable, all of which are obvious in view of Wong's statement that they plan to use relatively pure samples of known molecular weight or that encompass ions generated from molecules of substantially the same molecular weight and chemical identity in future experiments. *See* Wong at 550.
Claim 43	Claim 1 of the '538 patent	
A composition of matter comprising one or more populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species,	A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species,	Each element of claim 43 of the '726 patent is found in claim 1 of the '538 patent. Including the "calculation" or "determination" of the molecular weight from the values of mass/charge (m/z) step recited in claim 43 of the '726 patent is not only obvious, but also does not render the otherwise invalid claim

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		patentable. *See, e.g., Parker v. Flook*, 47 U.S. 548, 98 S.Ct. 2522 (1978).
the number of charges on each ion defining the ion's charge state number, each of said populations of multiply charged polyatomic ions comprising ions formed from one of said one or more distinct polyatomic parent molecular species,	the number of charges on said ions defining the ion's charge state number,	
at least one of said populations of ions comprising a plurality of sub-populations of ions, all the ions in each sub-population having the same charge state number,	said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number,	
said at least one of said populations comprising one such sub-population for each possible value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five,	said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five;	
said composition of matter being useful in the determination of a value of molecular weight for one or more of said distinct polyatomic parent molecular species, said determination of molecular weight being achieved by means of a mass analysis of ions from said one or more populations of ions and	carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and	
a calculation of the molecular weight values of said one or more polyatomic parent molecular species from the values of mass/charge (m/z) obtained by said mass analysis for	determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	

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the ions in said one or more populations of polyatomic ions.		
Claim 45, depends from claim 43	Claim 5 of the '538 patent	
The composition of matter of claim 43 in which said smallest value of charge state number is not less than seven and said largest value of charge state number is not less than ten.	(Claim 5, depends from claim 1) . . . wherein said minimum value of charge state number is not less than five and said maximum value is not less than ten.	Claim 45 of the '726 patent differs from claim 5 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 45 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 46, depends from claim 43	Claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 43 in which all molecules of any particular one of said distinct polyatomic parent molecular species have substantially the same molecular weight.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species. . . .	Claim 46 of the '726 patent recites that all the molecules of the species have "substantially the same molecular weight." Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same molecular weight. *See* Wong at 550.
Claim 47, depends from claim 43	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 43 in which at least one of said distinct polyatomic parent molecular species is selected from a class of compounds known as biopolymers.	(claim 21) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 47 of the '726 patent specifies that the "polyatomic parent molecular species" is a biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents suggests the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars,

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		and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 48, depends from 43	Claim 1 in view of Claim 27 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 43 in which at least one of said distinct polyatomic parent molecular species is selected from the group comprising proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins.	(claim 27, depends from claim 26, which depends from claim 20) . . . wherein at least one of said distinct polyatomic parent molecular species is chosen from the class known as biopolymers and comprising peptides, proteins, glycoproteins, carbohydrates and polynucleotides.	Claim 48 of the '726 patent adds to claim 43 that parent molecular species are "proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins." Not only does claim 27 of the '538 patent recite precisely this limitation, but such compounds are simply examples of the biopolymers disclosed by the '056 patent. *See* '056 Patent at 3:7-14.
Claim 49, depends from 43	Claim 1 in view of claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 43 in which at lease [sic] one of said distinct polyatomic parent molecular species is not selected from the group of synthetic polymers having less than four different distinct elemental constituent species, said group comprising poly (ethylene glycol)s.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species . . .	Claim 49 of the '726 patent excludes from claim 43 synthetic polymers such as PEG. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 50, depends from 43	Claim 1 in view of Claim 20 of the '538 patent or	

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	Claim 1 in view of the ’056 patent	
The composition of matter of claim 43 in which at least one of said distinct polyatomic parent molecular species has a molecular weight not less than 5000.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species	Claim 50 of the ’726 patent adds to claim 43 that the polyatomic parent molecular species has a “molecular weight not less than 5000.” Based on the specification of both patents, the term “polyatomic parent molecule” includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* ’538 Patent at 4:42-58. Moreover, claim 20 of the ’538 patent specifically recites the similar limitation of “at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000.” Furthermore, the ’056 patent teaches “the electrospray technique produces ions from solutes of very high molecular weights (e.g. 500,000).” *See* ’056 Patent at 3:7-14.
Claim 51	Claim 1	
The composition of matter comprising one or more populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species, the number of charges on each ion defining the ion's charge state number, each of said populations comprising ions formed from one of said one or more distinct polyatomic parent molecular species, at least one of said populations of	A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-	Claim 51 of the ’726 patent differs from claim 1 of the ’538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 51 of the ’726 patent is therefore not patentably distinct from the ’538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382. Including the “calculation” or “determination" of the molecular weight from the values of mass/charge (m/z) step recited in claim 51 of the ’726 patent is not only obvious, but also does not render the otherwise invalid claim patentable. *See, e.g., Parker v. Flook*, 47 U.S. 548, 98 S.Ct. 2522 (1978).

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multiply charged polyatomic ions comprising a plurality of sub-populations of ions, all the ions in each sub-population having the same charge state number, said same charge state number differing from the charge state numbers of the ion in the other sub-populations of said population, said charge state number having a value of at least five for all the ions in said at least one of said populations of multiply charged polyatomic ions, said composition of matter being useful for determining the molecular weight of one or more of said distinct polyatomic parent molecular species, said determination of the molecular weight being achieved by a mass analysis of the ions in said one or more populations of multiply charged polyatomic ions together with a calculation of the said molecular weight of said one or more polyatomic parent molecular species from the values of mass/charge (m/z) obtained by mass analysis of ions in said one or more populations of multiply charged polyatomic ions.	populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	
Claim 52, depends from claim 51	Claim 5 of the '538 patent	
The composition of matter of claim 51 in which every ion in said at least	(Claim 5, depends from claim 1) . . . wherein said minimum value of charge state number is not less than five and said maximum value is not less than ten.	Claim 52 of the '726 patent differs from claim 5 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a

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one of said populations of multiply charged polyatomic ions has a charge state number not less than seven.		prima facie case of obviousness exists and claim 52 of the ’726 patent is therefore not patentably distinct from the ’538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 57	Claim 1 in view of claim 20 of the ’538 patent or Claim 1 in view of the ’056 patent	
A composition of matter comprising	(claim 1) A method of determining the molecular weight of molecules comprising the steps of:	Claim 57 of the ’726 patent differs from claim 1 of the ’538 in that claim 57 of the ’726 patent includes steps related to the process by which the claimed compositions are generated. But the addition of a process or source limitation does not make a composition claim patentable if the composition itself is, as here, already in the prior art. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985); *see also* M.P.E.P. § 2113. Moreover, the electrospray ionization steps are recited by claim 20 of the ’538 patent. And the added process steps were known in the electrospray mass spectrometry art. *See, e.g.,* ’056 Patent at 2:53-60. Including the “calculated from the mass/charge (m/z) values of the multiply charged polyatomic ions produced from that species” language in claim 57 of the ’726 patent is not only obvious, but also does not render the otherwise invalid claims patentable. *See, e.g., Parker v. Flook*, 47 U.S. 548, 98 S.Ct. 2522 (1978).
one or more distinct populations of multiply charged polyatomic ions generated from a sample comprising one or more distinct polyatomic parent molecular species,	generating a population of multiply charged ions from a distinct polyatomic parent molecular species,	
the number of charges on each ion defining the ion's charge state number, each of said multiply charged polyatomic ions in any one of said one or more distinct populations having been formed from one of said distinct polyatomic parent molecular species in said sample,	the number of charges on said ions defining the ion's charge state number,	
at least one of said distinct populations of multiply charged polyatomic ions comprising a plurality of sub-populations of ions, all the ions in each sub-population of said plurality of sub-populations having the same charge state number,	said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number,	
said same charge state number differing from the charge state	said population including one sub-population for each possible integral value of charge state number extending	

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numbers of the ions in the other sub-populations of said plurality of sub-populations, said plurality of sub-populations comprising one such sub-population for each possible value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five, said composition of matter being formed by:	inclusively from a minimum of three to a maximum not less than five; . . . --- (claim 20) A method for producing a population of multiply charged ions . . . comprising the steps of: . . .	
dispersing a solution containing said polyatomic parent molecular species into a bath gas as charged droplets, said dispersing taking place in the presence of an electric field;	dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and	
allowing the solvent of said solution to evaporate from said charged droplets until at least some molecules of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged polyatomic ions;	allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions. ---	
said composition of matter having the property that the molecular weight of each of said distinct polyatomic parent molecular species in said sample can be calculated from the mass/charge (m/z) values of the multiply charged polyatomic ions produced from that species.	(claim 1 cont'd) carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	
Claim 59, depends from claim 51	Claim 1 of the '538 patent	
The composition of matter of claim	(claim 1)	Claim 59 of the '726 patent differs from claim

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51 in which said smallest value of charge state number is not less than seven and said largest value is not less than ten.	. . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five . . .	1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 59 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 60, depends from claim 51	Claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 51 in which all molecules of any particular one of said distinct polyatomic parent molecular species have substantially the same molecular weight**.**	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species;	Claim 60 of the '726 patent recites that all the molecules of the polyatomic parent molecular species have "substantially the same molecular weight." Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same molecular weight. *See* Wong at 550.
Claim 61, depends from claim 51	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 51 in which at least one of said distinct polyatomic parent molecular species is selected from the class of compounds known as biopolymers.	(claim 21, depends from claim 20) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 61 of the '726 patent specifies that the "polyatomic parent molecular species" is a biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents indicates that the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at

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		3:7-14.
Claim 62, depends from claim 51	Claim 1 in view of Claim 27 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 51 in which at least one of said distinct polyatomic parent molecular species is selected from the group comprising proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins.	(claim 27, depends from claim 26, which depends from claim 20) . . . wherein at least one of said distinct polyatomic parent molecular species is chosen from the class known as biopolymers and comprising peptides, proteins, glycoproteins, carbohydrates and polynucleotides.	Claim 62 of the '726 patent adds that the parent molecular species are "proteins, peptides, polypeptides, carbohydrates, oligonucleotides and glycoproteins." Not only does claim 27 of the '538 patent recite precisely this limitation, but such compounds are simply examples of the biopolymers disclosed by the '056 patent. *See* '056 Patent at 3:7-14.
Claim 63, depends from claim 51	Claim 1 in view of claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 51 in which at least one of said distinct polyatomic parent molecular species is not selected from the group of synthetic polymers comprising less than four different constituent elemental species, said group comprising poly (ethylene glycol)s.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species . . .	Claim 63 of the '726 patent excludes synthetic polymers such as PEG from claim 51. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 68	Claim 1 in view of claims 20 and 38 of the '538 patent or Claim 1 in view of the '056 patent	
A composition of matter that by mass analysis of its component ions is found to comprise one or more distinct populations of multiply charged polyatomic ions,	(claim 1) A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species,	Claim 68 of the '726 patent differs from claim 1 of the '538 patent in that it recites: that the charge state number of each subpopulation differs from the charge state number of the other sub-populations. This is obvious from claim 1 of the '538 patent. According to claim 1, the population of multiply charged

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the number of charges on each ion defining the ion's charge state number, each of said distinct populations of multiply charged polyatomic ions comprising ions having been formed from a polyatomic parent molecular species, at least one of said distinct populations of multiply charged polyatomic ions comprising a plurality of sub-populations of ions, all the ions in each sub-population having the same charge state number, said charge state number differing from the charge state number of the other sub-populations in said plurality of sub-populations, said plurality of sub-populations comprising one such sub-population for each possible value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five, said composition of matter being formed by: dispersing a solution containing one	the number of charges on said ions defining the ion's charge state number, said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number, ---------- (claim 38, depends from claim 34) whereby the ions of any arbitarily [sic] chosen one of said peaks in said sequence differ by one charge from the ions of the nearest peak whose ions are derived from identical molecules of the same said distinct polyatomic parent molecular species. ---------- (claim 1, cont’d) said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; ---------- (claim 20) A method for producing a population of multiply charged ions . . . comprising the steps of: . . . dispersing said solution as charged droplets into a bath	ions includes one subpopulation for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five. In other words, claim 1 of the ’538 patent includes subpopulations that each differ in charge state number from the other subpopulations. Furthermore, claim 38 of the ’538 patent recites a similar limitation. Claim 68 of the ’726 patent also differs from claim 1 of the ’538 in that claim 68 of the ’726 patent includes steps related to the process by which the claimed compositions are generated. But the addition of a process or source limitation does not make a composition claim patentable if the composition itself is, as here, already in the prior art. *See In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985); *see also* M.P.E.P. § 2113. Moreover, the Electrospray Ionization steps are recited by claim 20 of the ’538 patent. And the added process steps were known in the electrospray mass spectrometry art. *See, e.g.,* ’056 Patent at 2:53-60.

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or more polyatomic molecular species into a bath gas as charged droplets, said dispersing taking place in the presence of an electric field; allowing the solvent of said solution to evaporate from said charged droplets until at least some molecules of said polyatomic parent molecular species become dispersed in said bath gas as said multiply charged polyatomic ions; said mass analysis being carried out on a portion of said multiply charged polyatomic ions in said bath gas that is introduced into a vacuum system containing a mass analyzer.	gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions. ---------- (claim 1, cont'd) carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations.	
Claim 70, depends from claim 68	Claim 1 of the '538 patent	
The composition of matter of claim 68 in which said smallest value of charge state number is not less than seven and said largest value is not less than ten.	(claim 1) . . . said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five;	Claim 70 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 70 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 72, depends from claim 68	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 68	(claim 21)	Claim 72 of the '726 patent specifies that the "polyatomic parent molecular species" is a

INVALIDITY CLAIM CHART A
U.S. PATENT NO. 5,686,726 ('538 Patent in view of Wong and/or '056 Patent)

5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
in which at least one of said distinct polyatomic parent molecular species in said solution is selected from a class of compounds known as biopolymers.	. . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents indicates the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 73, depends from claim 68	Claim 20 of the '538 patent Claim 1 in view of the '056 patent	
The composition of matter of claim 68 in which at least one of said distinct polyatomic parent molecular species in said solution has a molecular weight not less than 5000.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species. . . .	Claim 73 of the '726 patent adds that the polyatomic parent molecular species has a "molecular weight not less than 5000." Based on the specification of both patents, the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* '538 Patent at 4:42-58. Moreover, claim 20 of the '538 patent specifically recites the similar limitation of "at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000." Furthermore, the '056 patent teaches "the electrospray technique produces ions from solutes of very high molecular weights (e.g. 500,000)." *See* '056 Patent at 3:7-14.
Claim 74	Claim 1 in view of claims 20 and 38 of the '538 patent or Claim 1 in view of Wong	
A composition of matter derived from a sample comprising	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three	Claim 74 of the '726 patent differs from claim 1 of the '538 patent in reciting that the polyatomic parent molecular species has "substantially the same molecular weight and

INVALIDITY CLAIM CHART A
U.S. PATENT NO. 5,686,726 ('538 Patent in view of Wong and/or '056 Patent)

5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
	charges per ion, comprising the steps of:	chemical identity." This is obvious over claim 1 of the '538 patent, which requires that the molecules of the distinct molecular species have substantially the same molecular weight or formula or be otherwise indistinguishable. This is also recited by claim 20 of the '538 patent. Moreover, Wong also states that they plan to use relatively pure samples of known molecular weight or that encompass ions generated from molecules of substantially the same molecular weight and chemical identity in future experiments. *See* Wong at 550. Furthermore, claim 74 of the '726 patent adds that the "distinct polyatomic parent molecular species having substantially the same molecular weight and chemical identity," a version of the limitation requiring that the molecules of the distinct molecular species have substantially the same molecular weight or formula or are otherwise indistinguishable. Not only is this disclosed by claim 20 of the '538 patent, but Wong shows that it was known in the art to use mass spectrometry to determine the molecular weight of a purified compound, i.e., a population of molecules having substantially the same molecular weight and chemical identity. *See* Wong at 550. In fact, Wong, which is a prior art publication describing the application of electrospray ionization techniques to solutions of polyethylene glycols, states that, "[i]n future experiments, we plan to use relatively pure samples of known molecular weight." *Id.*
one or more distinct polyatomic parent molecular species, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and chemical identity, said composition of matter comprising one or more distinct populations of polyatomic ions, at least one of said distinct populations of ions comprising multiply charged ions formed from one of said one or more distinct polyatomic parent molecular species in said sample, the number of charges on each ion defining the charge state number of that ion, each of said populations of multiply charged ions having the property that when its ions are mass analyzed they give rise to a mass spectrum comprising a multiplicity of peaks, said multiplicity of peaks comprising at least one coherent sequence of peaks,	p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species . . . . ---------- (claim 34) A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number, ---------- (claim 38, depends from claim 34) A method of determining the molecular weight of a distinct polyatomic parent molecular species comprising: generating a mass spectrum comprising a sequence of discrete peaks due to multiply charged ions of said distinct polyatomic parent molecular species, each of said multiply charged ions having at least three charges; . . . . ---------- (claim 38)	

INVALIDITY CLAIM CHART A
U.S. PATENT NO. 5,686,726 ('538 Patent in view of Wong and/or '056 Patent)

5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
the ions of each peak in said coherent sequence having the same charge state number, said charge state number being greater thorn [sic] unity and differing by one unit from the charge state numbers of the ions of each immediately adjacent peak in said coherent sequence, said coherent sequence of peaks comprising one peak for each different value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five.	. . . wherein said step of analyzing said sequence of discrete peaks of said spectrum includes uses the mass/charge (m/z) values of at least two of said peaks in said sequence of discrete peaks, said sequence of discrete peaks having a coherence whereby the ions of any arbitarily [sic] chosen one of said peaks in said sequence differ by one charge from the ions of the nearest peak whose ions are derived from identical molecules of the same said distinct polyatomic parent molecular species. ---------- (claim 1 continued) said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; . . .	Additionally, claim 74 of the '726 patent recites "a multiplicity of peaks comprising at least one coherent sequence of peaks." Not only does claim 38 the '538 patent also recite at least one coherent sequence of peaks, but Wong shows multiply charged ions that give rise to a mass spectrum comprising multiple peaks that have at least one coherent sequence of peaks. *See* Wong at 548. Wong also shows, as recited by claim 74 of the '726 patent, that the "charge state number being greater thorn [sic] unity." *See* Wong at 548. Moreover, this property is inherent in claim 1 of the '538 patent, which recites that the population of multiply charged ions includes one subpopulation for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five. For example, if one subpopulation has a charge state number of three, the next subpopulation would have a charge state number of four, and the next subpopulation would have a charge state number of five, and so on.
Claim 76, depends from claim 74	Claim 1 in view of claim 21 of the '538 patent or Claim 1 of the '538 patent in view of the '056 patent	
The composition of matter of claim 74 in which at least one of said distinct polyatomic parent molecular species is selected from a class of compounds known as biopolymers.	(claim 21) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 76 of the '726 patent specifies that the "polyatomic parent molecular species" is a biopolymer. Not only does claim 21 of the '538 patent recite the same, but the specification of both patents suggests the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides. *See, e.g.,* '538 Patent

INVALIDITY CLAIM CHART A
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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
		at 4:42-58. Moreover, it would have been obvious in view of the '056 patent to apply the method of claim 1 of the '538 patent to biopolymers. *See* '056 Patent at 3:7-14.
Claim 77, depends from claim 74	Claim 1 in view of claim 20 of the '538 patent or Claim 1 of the '538 patent in view of Wong	
The composition of matter of claim 74 in which at least one of said distinct polyatomic parent molecular species is not selected from the group comprising poly (ethylene glycol)s.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species	Claim 77 of the '726 patent excludes compounds such as PEG from claim 74. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 78, depends from claim 74	Claim 1 in view of claim 20 of the '538 patent or Claim 1 in view of the '056 patent	
The composition of matter of claim 74 in which at least one of said distinct polyatomic parent molecular species has a molecular weight not less than about 5000.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species. . . .	Claim 78 of the '726 patent adds that the polyatomic parent molecular species has a "molecular weight not less than about 5000." Based on the specification of both patents, the term "polyatomic parent molecule" includes biopolymers like proteins, complex sugars, and polynucleotides—molecules known in the art to have molecular weights greater than 5000 Daltons. *See, e.g.,* '538 Patent at 4:42-58. Moreover, claim 20 of the '538 patent specifically recites the similar limitation of "at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000." Furthermore, the '056 patent teaches "the electrospray technique produces ions from solutes of very

INVALIDITY CLAIM CHART A
U.S. PATENT NO. 5,686,726 ('538 Patent in view of Wong and/or '056 Patent)

5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
		high molecular weights (e.g. 500,000)." *See* '056 Patent at 3:7-14.
Claim 101	Claim 20 of the '538 patent alone or in view of Wong	
A composition of matter comprising one or more populations of polyatomic gaseous ions, at least one of said populations comprising multiply charged ions formed from the same chemically distinct parent species of polyatomic neutral molecules, said same chemically distinct species of polyatomic neutral molecules not including synthetic polymers such as poly (ethylene glycol)s, all of said multiply charged ions, formed from said same chemically distinct species of polyatomic neutral molecules, having at least three charges.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species; dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions.	Claim 101 of the '726 patent includes the term, "gaseous ions." This, however, is obvious over the method of Claim 20 of the '538 patent which: (1) disperses a solution containing the parent molecular species into a gas as charged droplets in the presence of an electric field; and (2) allows the solvent to evaporate into a gas. Additionally, Claim 101 of the '726 patent adds excludes compounds such as PEG. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 103, depends from claim 101	Claim 26 of the '538 patent	
A composition of matter according to claim 101 in which all of said multiply charged polyatomic ions, formed from, said chemically distinct species of polyatomic neutral molecules, have	(claim 26, depends from 20) . . . wherein all members of said population with molecular weights greater than 5000 have at least five charges per ion.	Claim 103 of the '726 patent differs from claim 26 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 103 of the '726 patent is therefore not patentably distinct from the '538

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
at least seven charges.		patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 104	Claim 1 in view of claims 20 and 19 of the '538 patent or Claim 1 in view of the '056 patent and Wong	
A composition of matter comprising one or more populations of polyatomic gaseous ions, at least one of said populations of polyatomic ions comprising multiply charged ions formed from the same chemically distinct parent species of polyatomic neutral molecules, said chemically distinct parent species of polyatomic molecules not being selected from the class comprising oligomers of synthetic polymers such as poly (ethylene glycol)s, the number of charges on each ion defining the charge state number of that ion, said at least one of said populations	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species; dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions. ---------- (claim 1) A method of determining the molecular weight of molecules comprising the steps of: generating a population of multiply charged ions from a distinct polyatomic parent molecular species, the number of charges on said ions defining the ion's charge state number,	Claim 104 of the '726 patent differs from claim 1 of the '538 patent in that claim 104 recites the term, "gaseous ions." This, however, is obvious over Claim 20 of the '538 patent which: (1) disperses a solution containing the parent molecular species into a gas as charged droplets in the presence of an electric field; and (2) allows the solvent to evaporate into a gas. Furthermore, the use of gaseous ions is known in the prior art, as exemplified by the '056 patent, which describes standard electrospray ionization. *See* '056 Patent at 2:54-60. The term "*chemically* distinct parent species of polyatomic neutral molecules" in claim 104 does not render that claim patentably distinct from claim 1 of the '538 patent, which recites "a distinct polyatomic parent molecular species." Moreover, claim 19 of the '538 patent recites similar language ("distinct polyatomic parent molecular species is chemically distinct"). Additionally, Claim 104 of the '726 patent excludes compounds such as PEG. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight"

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
of polyatomic multiply charged ions comprising a plurality of sub-populations, one such sub-population for each possible integral value of charge state number beginning with a smallest value not less than three and extending to a largest value not less than five.	said population of ions comprising a plurality of sub-populations, the ions of each sub-population having the same charge state number, said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five; carrying out a mass analysis of the ions in said population and from the results of said mass analysis obtaining mass/charge (m/z) values for said ions of said sub-populations; and determining a value of the molecular weight of said distinct polyatomic parent molecular species from the mass/charge (m/z) values of said ions of said sub-populations. ---------- (claim 19 depends from claim 1) . . . wherein said distinct polyatomic parent molecular species is chemically distinct.	instead of polyethylene glycols. Wong at 550.
Claim 105, depends from claim 104	Claim 1 of the '538 patent	
A composition of matter according to claim 104 in which said smallest value of charge state number is not less than five and said largest value is not less than seven.	(claim 1) . . .said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five;	Claim 105 of the '726 patent differs from claim 1 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 105 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 106, depends from claim 104	Claim 1 of the '538 patent	
A composition of matter according to claim 104	(claim 1)	Claim 106 of the '726 patent differs from claim 1 of the '538 patent in the range of

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
in which said smallest value of charge state number is not less than seven and said largest value is not less than ten.	. . .said population including one sub-population for each possible integral value of charge state number extending inclusively from a minimum of three to a maximum not less than five;	charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 106 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 107	Claim 21 of the '538 patent (depends from claim 20) alone or in view of Wong	
A composition of matter comprising one or more populations of polyatomic gaseous ions, all of the ions in at least one of said populations comprising multiply charged polyatomic ions having a net charge equal to or greater than three elementary charges and a composition characterized by the empirical chemical formula (Cc Hh Nn Oo Ss Pp Tt Uu Vv Ww Yy) wherein upper case letters C, H, N, O, S, P stand respectively for the elements Carbon, Hydrogen, Nitrogen, Oxygen, Sulfur, Phosphorous and T, U, V, W, Y each stand for other elements in the Periodic Table, the lower case subscript letters associated with each of said upper case letters symbolizing an integer equal to the number of atoms of the corresponding element in said ion, all the ions with three or more charges in at least one of said one or	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species; dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions. ---------- (claim 21 depends from 20) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class	Claim 107 of the '726 patent includes the term, "gaseous ions." This, however, is obvious over the method of Claim 20 of the '538 patent (and therefore from claim 21, which depends therefrom) which: (1) disperses a solution containing the parent molecular species into a gas as charged droplets in the presence of an electric field; and (2) allows the solvent to evaporate into a gas. The recitation by claim 107 that the "net charge [is] equal to or greater than three elementary charges" does not render claim 107 patentably distinct from claim 21 of the '538 patent, which provides for a population of multiply charged ions where all members have "at least three charges per ion." Additionally, claim 107 recites the elements present in the composition of matter according to an empirical chemical formula, "Cc Hh Nn Oo Ss Pp Tt Uu Vv Ww Yy", and the "number of different subscripts c, h, o, n, p, s, t, u, v, w, y having values greater than zero is five or less." This property is obvious over claim 21 of the '538 patent, which recites that the polyatomic parent molecular

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
more populations of ions having compositions such that the number of different subscripts c, h, o, n, p, s, t, u, v, w, y having values greater than zero is five or less, said ions not being derived from a member of the class of synthetic polymers that include poly (ethylene glycol)s.	comprising biopolymers.	species is a biopolymer [*see* claim 27 of the '538 patent]. Therefore, claim 21 of the '538 patent discloses a species (e.g., carbohydrates or polynucleotides) of the genus recited in claim 107 of the '726 patent. *See In re Goodman*, 11 F.3d at 1053 (an earlier species claim anticipates and therefore is not patentably distinct from a later genus claim). Claim 107 of the '726 patent excludes compounds such as PEG. Claim 20 of the '538 patent recites a similar feature that excludes the class of compounds that includes PEG—"a structure that cannot be represented as a polymer of a single monomeric species." Wong also teaches that future experiments will use "relatively pure species of known molecular weight" instead of polyethylene glycols. Wong at 550.
Claim 108, depends from claim 107	Claim 21 of the '538 patent	
A composition of matter as in claim 107 in which all the ions in said at least one population of multiply charged polyatomic ions have at least five charges.	(claim 21, depends from claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion	Claim 108 of the '726 patent differs from claim 21 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 108 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 109, depends from claim 107	Claim 21 of the '538 patent	
A composition of matter as in claim 107 in which all the ions in said at least one population of multiply charged	(claim 21, depends from claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a	Claim 109 of the '726 patent differs from claim 21 of the '538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the

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5,686,726	'538 Patent	Basis of Invalidity Contention (incl. in view of Wong and/or the '056 patent)
polyatomic ions have at least seven charges.	molecular weight greater than 5000 have at least three charges per ion	prior art, a prima facie case of obviousness exists and claim 109 of the '726 patent is therefore not patentably distinct from the '538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 110	Claim 21 of the '538 patent.	
A composition of matter comprising one or more populations of gaseous ions, at least one of said populations comprising multiply charged polyatomic ions having a net charge equal to or greater than three elementary charges and a composition characterized by the empirical chemical formula (Cc Hh Nn Oo Ss Pp Tt Uu Vv Ww Yy) wherein upper case letters C, H, N, O, S, P stand respectively for the elements Carbon, Hydrogen, Nitrogen, Oxygen, Sulfur, Phosphorous and T, U, V, W, Y each stand for other elements in the Periodic Table, the lower case letters symbolizing an integer equal to the number of atoms of the corresponding element in said ion, all the ions with three or more charges in at least one of said one or more populations of polyatomic ions having compositions such that the number of different subscripts c, h, n, o, p, s, t, u, v, w, y having values greater than zero is greater than five.	(claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion, comprising the steps of: p1 supplying a solution containing as a solute at least one distinct polyatomic parent molecular species with a molecular weight greater than 5000, all molecules of each of said distinct polyatomic parent molecular species having substantially the same molecular weight and a structure that cannot be represented as a polymer of a single monomeric species; dispersing said solution as charged droplets into a bath gas, said dispersion taking place in the presence of an electric field; and allowing the solvent of said solution to vaporize from said charged droplets into said bath gas until at least some molecules of at least one of said distinct polyatomic parent molecular species become dispersed in said bath gas as said multiply charged ions. --- (claim 21, depends from claim 20) . . . wherein at least one of said distinct polyatomoic [sic] parent molecular species is chosen from the class comprising biopolymers.	Claim 110 of the '726 patent includes the term "gaseous ions." This, however, is obvious over the method of Claim 20 of the '538 patent (and therefore from claim 21, which depends therefrom) which: (1) disperses a solution containing the parent molecular species into a gas as charged droplets in the presence of an electric field; and (2) allows the solvent to evaporate into a gas. The limitation of claim 110 of "net charge equal to or greater than three elementary charges" does not render claim 110 patentably distinct from claim 21 of the '538 patent, which provides for a population of multiply charged ions where all members have "at least three charges per ion." Additionally, claim 110 recites the elements present in the composition of matter according to an empirical chemical formula, "Cc Hh Nn Oo Ss Pp Tt Uu Vv Ww Yy", and the "number of different subscripts c, h, o, n, p, s, t, u, v, w, y having values greater than zero is five or less" This property is obvious over claim 21 of the '538 patent, which recites that the polyatomic parent molecular species is a biopolymer [*see* claim 27 of the '538 patent]. Therefore, claim 21 of the '538 patent discloses a species (e.g., carbohydrates or polynucleotides) of the

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		genus recited in claim 110 of the ’726 patent. *See In re Goodman*, 11 F.3d at 1053 (an earlier species claim anticipates and therefore is not patentably distinct from a later genus claim).
Claim 111, depends from claim 110	Claim 21 of the ’538 patent.	
A composition of matter as in claim 110 in which all the ions in said at least one population of multiply charged polyatomic ions have at least five charges and a composition such that the number of different subscripts c, h, n, o, p, s, t, u, v, w, y having values greater than zero is greater than five.	(claim 21, depends from claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion	Claim 111 of the ’726 patent differs from claim 21 of the ’538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 111 of the ’726 patent is therefore not patentably distinct from the ’538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.
Claim 112, depends from 110	Claim 21 of the ’538 patent.	
A composition of matter as in claim 110 in which all the ions in said at least one population of multiply charged polyatomic ions have at least seven charges and a composition such that the number of different subscripts c, h, n, o, p, s, t, u, v, w having values greater than zero is greater than five.	claim 21, depends from claim 20) A method for producing a population of multiply charged ions, wherein all members of said population with a molecular weight greater than 5000 have at least three charges per ion	Claim 112 of the ’726 patent differs from claim 21 of the ’538 patent in the range of charge states recited. Where the range recited in a claim overlaps or lies within the prior art, a prima facie case of obviousness exists and claim 112 of the ’726 patent is therefore not patentably distinct from the ’538 patent. *See In re Wertheim*, 541 F.2d at 267*; In re Peterson*, 65 U.S.P.Q.2d at 1382.